The University of Chicago

PART I: A STUDY OF ORGANIC OXIDES
PART II: STABILITY OF ORGANO LEAD DERIVATIVES

A DISSERTATION SUBMITTED TO THE
GRADUATE FACULTY IN CANDIDACY FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY
1929

By
HOUGHTON GEORGE CLAPP

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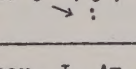
INTRODUCTION

A recent paper by Kharasch and Marker[1] gives a table of the relative degree of electronegativity of a number of organic radicals. These authors define electronegativity as the attraction of the radicals for their valence electrons. The radicals which hold their electrons the most firmly are the most electronegative. Furthermore, it is pointed out that these groups have the power of altering the electronegativity of a carbon atom to which they are attached. It is shown that the methyl group has a certain attraction for its valence electrons, and is a moderately strong electronegative group. If now a phenyl group is substituted for a hydrogen atom the valence electrons are displaced further from the methyl carbon atom, and, therefore, the benzyl radical is less electronegative than the methyl radical. If a second phenyl radical is attached, the displacement becomes still greater. If a third phenyl radical is now introduced, the valence electrons of the methyl carbon atom move out to a position so far removed from their nucleus, that two such radicals, when attached to one another form an extremely weak bond and the molecule readily dissociates into two radicals.

This hypothesis lends itself, moreover, to the prediction of addition reactions to compounds containing a double bond. If the electronegativity of the radicals R and R' attached to a double bond are known, and since the effect of these groups on the valence electrons of the adjacent carbon is known, the position of the second pair of electrons in the double bond may be readily predicted. Thus if we have a compound of the nature $RC(H)=C(H)R'$, in which R is more strongly electronegative than R', the electrons will be displaced further from the carbon atom holding R', the less electronegative group, with the net result that the valence pair will be displaced towards the weaker group, thus:



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[1] Kharasch and Marker, J. Am. Chem. Soc., 48, 3130 (1926).

These facts are brought out by Kharasch and Darkis[2] who, making use of the theory go one step further, and argue therefrom that if two groups of marked difference in electronegativity are adjacent to the double bond the electrons are displaced towards the weaker group. There should, therefore, be a case in which the difference of the electronegativity of the two radicals is so small that if the electrons were on one side away from the normal position, little external energy should be required to cause a replacement to the normal position, and an equimolecular mixture of isomers should result from the addition of an halogen acid. This theory rendered it possible to select a compound whose nature was such as to allow the formation of two products.

By the same line of reasoning it should be possible to prepare an oxide which would be capable of reacting in two ways.

With this objective in mind a review of the literature of oxides was made. It was desired to ascertain whether the reactions reported agreed with the theory of partial polarity, and to determine the best methods and compounds to employ in the study of electroisomerism of oxides. In this preliminary study, however, it was found that there were so many reactions reported which seemed to conflict with each other, and so many results which seemed anomalous when compared with the theory that it was decided to study the whole subject, to determine if there was any common basis upon which these reactions might be generalized, and to find if possible some reagent which would yield comparable results with the various types of oxides.

METHODS OF PREPARATION OF OXIDES

Naturally the first aspect of the problem which was attacked was to determine the best method of preparation, not alone from the standpoint of ease of procedure, but also from considerations of the purity of the final product. There have been three general methods reported for the preparation of oxides. Two of these methods are based upon the formation of the halohydrines, and subsequent treatment in such a manner as to split off a molecule of halogen acid, leaving the oxide. The third method depends upon the use of a hydroperoxide which produces the oxide by the oxidation of a double bond.

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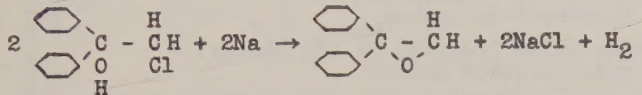
[2]Kharasch and Darkis, Chem. Revs., 5, 571 (1928).

Wurtz[3] was the first to prepare an oxide by the halohydrine method. He prepared ethylene chlorohydrine from ethylene glycol and hydrochloric acid. This material was then treated with aqueous potassium hydroxide. Tiffeneau and Fourneau[4] improved the method considerably in that they used hypoiodous acid prepared from mercuric oxide and iodine. The second step of their reaction was brought about in ether solution, using powdered potassium hydroxide to remove the hydrogen iodide. The yields claimed for this method were about 50 per cent of the calculated amount.

A second method developed by Tiffeneau[5] substituted sodium metal for the potassium hydroxide. Otherwise the essential details of the method were not altered. The reaction probably proceeds in the following manner:



A third method for the preparation of oxides was developed by Prileschajew.[6] This method involves the interaction of the unsaturated compound and benzoylhydroperoxide in ether or chloroform solution, preferably the latter. The yields in the cases reported were quite high, and the reaction appeared to be of general applicability.

In order to determine which method would be the best to employ in the work, it was decided to prepare some styrene oxide by two of the most convenient of the above methods, namely the potassium hydroxide-halohydrine method and the benzoyl hydroperoxide method. In the first case a water solution of hypobromous acid was prepared, and allowed to react with styrene. The styrene bromohydrine so prepared was then extracted with ether, washed free of bromine, dried, and allowed to react with powdered potassium hydroxide. The material was washed, dried, and the oxide obtained by the removal of the ether. The oxide was fractionated first in vacuo and finally at atmospheric pressure. The fraction which boiled between 188-189° constituted the major portion of

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[3]Wurtz, Ann., 110 (1859); Ann. Chim. Phys. 3e, 55, 427 (1859).

[4]Tiffeneau and Fourneau, Compt. rend., 140, 1595 (1905).

[5]Tiffeneau, Compt. rend., 140, 1458 (1905).

[6]Prileschajew, Ber., 42, 4811 (1909); 43, 959 (1910); Chem. Zentr., 1, 1279 (1911).

the distillate and was assumed to be the oxide sought.

In the case of the benzoyl hydroperoxide method, the directions in "Organic Syntheses"[7] were followed carefully. The chloroform was distilled off and the oxide fractionated first in vacuo, and then at atmospheric pressure. The major portion of this material distilled over between 188-189°.

The two samples of the oxides prepared as described above were, therefore, identical as far as the boiling point was concerned, although prepared by different methods. But the material which had been prepared from the styrene bromohydrine still retained sufficient halogen to give a faint Beilstein test. Furthermore, upon examination of the two samples by means of the refractometer quite different readings were obtained:

Styrene Oxide prepared by the bromohydrine method	N_D^{20} 1.5357
Styrene Oxide prepared by the benzoyl hydroperoxide method	N_D^{20} 1.5397
Water	N_D^{20} 1.3333

From these results it may be seen that although the oxide prepared by the bromohydrine method was presumably purer than that previously obtained by Tiffeneau and Fourneau,[8] who collected the fraction between 188-192°, nevertheless, the materials prepared by the different methods did not check each other in refractive indices. It seems quite probable, therefore, that the oxides which these investigators prepared from the halohydrines may not have been quite pure. Furthermore, it was found that on repeating the preparation of the styrene oxide by the benzoyl hydroperoxide method, the product obtained gave the same refractive index (N_D^{20} 1.5397) which had been obtained previously. To be sure Tiffeneau reports the molecular refractivity of his oxide, but gives no data as to how it was obtained or computed. As there are several formulae for this computation this particular constant was valueless as a check.

REACTIONS OF OXIDES

The reactions which oxides undergo may be conveniently classified into three groups:[9]

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[7] "Organic Syntheses," 8, 30, 102.

[8] Tiffeneau and Fourneau, Compt. rend., 140, 1595 (1905).

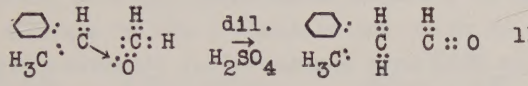
[9] The reactions of the oxides with bases has been purposely omitted. These reactions will be investigated more fully and reported on at a future date.

1. Decomposition with acids
2. Decomposition with salts
3. Decomposition with the Grignard reagent

Each of the above types of reaction will be discussed, and it will be shown whether or not they agree with the theory of partial polarity.

DECOMPOSITION WITH ACIDS

In the case of the decomposition with acids, the reaction may proceed in one of three ways. The presence of acid, such as dilute sulfuric acid, may cause the oxide to rearrange to the corresponding ketone or aldehyde. Such a reaction is mentioned by Tiffeneau[10] in the case of unsymmetrical methyl phenyl ethylene oxide:



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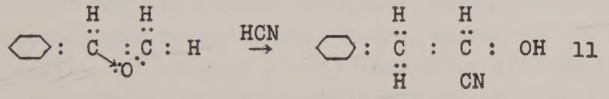
A similar reaction is cited by the same worker[12] in the case of hydrogen cyanide, but in this case the acid adds on after the rearrangement to give the cyanhydrine, thus:



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A second reaction induced by dilute acids such as sulfuric acid is the hydrolysis of the oxide to the corresponding glycol. As an example of this may be cited the work of Prileschajew[13] with tetramethyl ethylene oxide, which upon treatment with dilute sulfuric acid undergoes hydrolysis, yielding the corresponding tetramethyl ethylene glycol, or pinnacol, thus:

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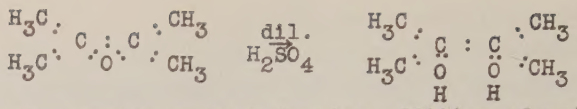
[10] Tiffeneau, Compt. rend., 140, 1458 (1905).

[11] For the interpretation of this rearrangement consult p. 12. Note particularly that these rearrangements occur most readily when strongly electronegative groups are present. These groups displace the electrons so far from the carbon atom toward the oxygen atom that the application of a small amount of energy brings about the rearrangement. The correctness of this hypothesis is borne out by the facts that rearrangement of oxides containing weakly electronegative groups takes place with great difficulty or not at all.

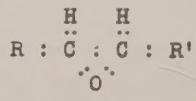
[12] Tiffeneau, Compt. rend., 146, 236 (1908).

[13] Prileschajew, Chem. Zentr., 2, 268 (1911).

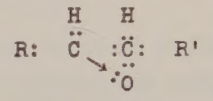


Since, however, reactions which involve addition of water to the oxides yield symmetrical products, they are no criteria in evaluating the concepts advanced.

The third type of reaction with acids is the most interesting and at the same time the most important from a theoretical aspect. In these reactions the oxide adds a molecule of the halogen acid yielding the corresponding halohydrine. According to the theory of partial polarity it should be possible to predict the manner of this addition, since it would be determined by the relative position of the electrons in the oxygen-carbon bond. If we take the case of a simple substituted ethylene oxide of the type indicated below in which the radicals R and R' are the same, obviously the oxide will have a symmetrical structure (Type I).

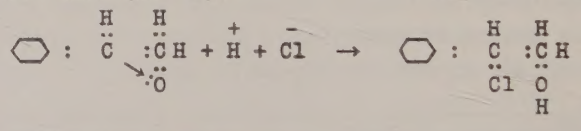


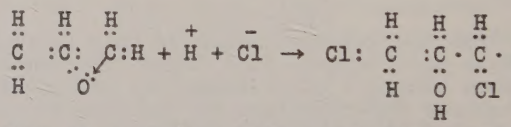
Type I



Type II

But if the radical R is more electronegative than R', the electrons around the oxygen are no longer symmetrically placed and the electrons will move away from R towards the oxygen, weakening the bond at this point (Type II). If, now, a molecule of halogen acid is allowed to react, the bond will open at its weakest point, the halogen going to the carbon atom and the hydrogen to the to the oxygen atom thus (Ex. I):

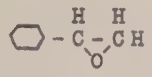
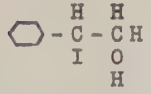
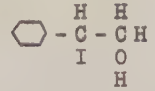
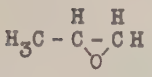
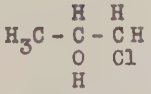
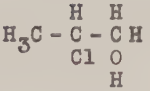
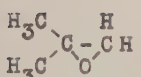
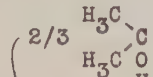
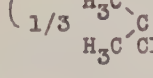
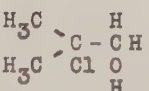
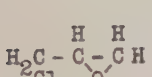
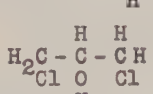
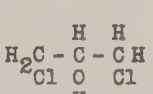
(Ex. I) 

(Ex. II) 

The case of substitution of a more positive radical is also shown to have just the opposite effect (Ex. II).

With the above facts in mind some examples of the addition of halogen acids reported in the literature will be given. The addition products obtained are given in the first column while in the second column are those which theoretically should have

been formed:

	Oxide used	Product found	Predicted product	
(1)				14
(2)				15, 16
(3)		2/3  1/3 		17, 18
(4)				19

It will be seen that in the above table, reactions 1 and 4 were predicted correctly, and for reaction 3 Henry reports the reaction going only in the direction predicted by the theory, although Michael reports the amounts of each isomer as shown.

REACTIONS OF OXIDES WITH SALTS

The decomposition of oxides with salts may proceed in either of two ways. Certain salts such as zinc chloride possess

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[14] Tiffeneau and Fourneau, Compt. rend., 146, 697 (1908).

[15] Michael, Ber., 39, 2785 (1906). Henry, Rec. Trav. Chim., 22, 325 (1905).

[16] While this reaction appears at first to be in conflict with the theory it may still be in accordance with the concept due to the method of preparation.

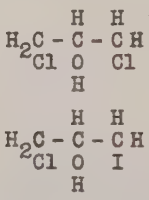
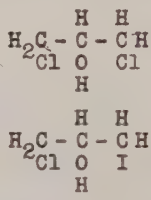
[17] Michael, Jr. Pr. Ch. (2), 64, 102 (1901); Ber., 39, 2789 (1906). Henry, Compt. rend., 142, 129 (1906); Ber., 39, 3677 (1906).

[18] This reaction was carried out by both Michaels and Henry. Henry found that if the reaction was carried out with the evolution of heat, mainly the second product was formed. Michaels, on the other hand, had carried out the addition at low temperature, and as he prepared his material from the 1-chloro isobutanol-2, by the action of KOH, some of this product might be expected. Moreover, as the yields were not 100 per cent, and 2-chloro isobutanol-1 decomposes very readily it is possible that he actually obtained 50 per cent of each product.

[19] Henry, Compt. rend., 142, 493 (1906).

the property of causing the rearrangement to the isomeric aldehyde or ketone form. Krassouski[20] gives a rather far-fetched explanation for this reaction, based upon Baeyer's theory of oxonium salts. However, this reaction is easy to comprehend on the basis that the aldehyde or ketone is the stable form of the compound, and that the salt plays the role of a catalyst in speeding up the transformation which is already proceeding very slowly.

The second type of reaction is between salts of the type $MgBr_2$, which yield bromo hydrines. These reactions are also explained by Grignard[21] on the basis of oxonium salts, but this seems entirely unnecessary in this case. It would be much simpler to assume the hydrolysis of the magnesium salt into the corresponding halogen acid, which then adds to the oxide in the normal manner. In the reactions cited below the reaction products isolated are identical with those which would be predicted upon a theoretical basis, if the reaction consisted merely of the addition of the corresponding halogen acids. As examples of the reactions just discussed the following may be given:

Oxide	Reaction Product	Theoretical Product from HX addition	Reference
			22

REACTIONS OF THE GRIGNARD REAGENT

From a study of the reactions of oxides which have been given it is obvious that none of the reagents employed are well suited to the purpose of determining the electronic structure of the oxides, by means of identification of their addition products. The Grignard reagent, however, is admirably adapted for such a study. Not only are the addition products readily identifiable in most cases, but the nature of the Grignard reagent may be varied at will. Furthermore, while the Grignard reagent is generally regarded to dissociate in one direction only, in reality, there

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[20] Krassouski, Chem. Zentr., 2, 348 (1906).

[21] Grignard, Bull. Soc. Chim., 3e, 29, 944 (1903).

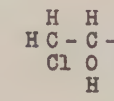
[22] Ibid.

are two possibilities, thus:

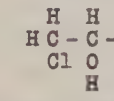
$$R\overset{+}{M}g + \overset{-}{X} \rightleftarrows RMgX \rightleftarrows \overset{-}{R} + \overset{+}{M}gX$$

depending upon the relative electronegativity of R and X, and the nature of the radicals R and X will determine whether the dissociation proceeds in one direction or the other.

These notions clear up the work done on epichlorhydrine by Iositsch,[23] Kling,[24] and Tiffeneau.[25] Iositsch claimed at first to have obtained both a chloro amyl alcohol, $C_5H_{11}OCl$, and glycerine chlorobromohydrine:

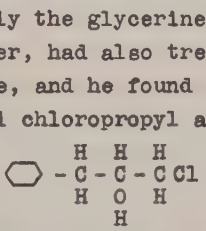


Kling repeated this work using methyl magnesium iodide, and obtained only the glycerine chloroiodohydrine:

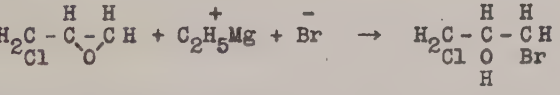


Finally Tiffeneau repeated the work using methyl, ethyl, and propyl magnesium bromides, and he was able to isolate none of the higher alcohols, but only the glycerine halohydrine.

Iositsch, however, had also treated epichlorhydrine with phenyl magnesium bromide, and he found that this reagent added to the oxide, giving phenyl chloropropyl alcohol:



This work was repeated and confirmed by Tiffeneau. These reactions are readily explainable from the standpoint of the theory of partial polarity. This shows that it is merely due to the dissociation of the bromine in one case, and the dissociation of the phenyl group in the other:



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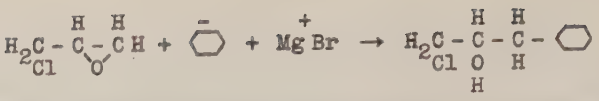
[23] Iositsch, J. Soc. Phys. Chim. Russ., 34, 36 (1902); 36, 6 (1904).

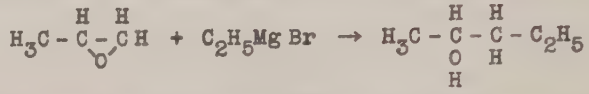
[24] Kling, Bull. Soc. Chim., 3e, 31, 14 (1904).

[25] Tiffeneau and Fourneau, Bull. Soc. Chim., 4e, 1, 1227 (1907).

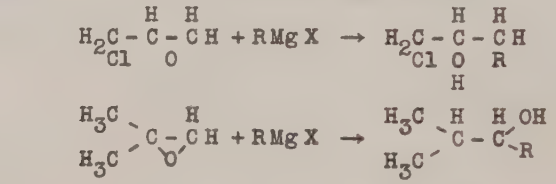


The same reaction was also observed by Tiffeneau in the case of the Grignards prepared from p-bromoanisole and benzyl chloride.[26] In the latter case the yield of alcohol was a little over 50 per cent, while the yield of glycerine chlorobromo hydrine was 25 per cent.

Henry[27] investigated the reaction between propylene oxide and ethyl magnesium bromide. He found that the reaction proceeded only upon heating the reaction mixture. He stated that the reaction went in the following manner, yielding a pentanol-2:[28]



Tiffeneau and Fourneau,[29] basing their conclusions on the reactions of epichlor hydrine, advanced the following theory. Monosubstituted oxides react with reagents in a manner similar to ethylene oxide, while disubstituted oxides react as if they had first isomerized to the corresponding aldehyde:



Shortly after, these workers[30] attempted to verify this supposition. They used styrene oxide as an example of a monosubstituted oxide. Upon treatment with methyl and ethyl magnesium bromides, they found that it had reacted as if it had tautomerized to the aldehyde. They then abandoned their first theory and concluded that aryl and alkyl substituted oxides differ in their

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[26] While it is stated that these products are formed, it is unfortunate that they were not identified.

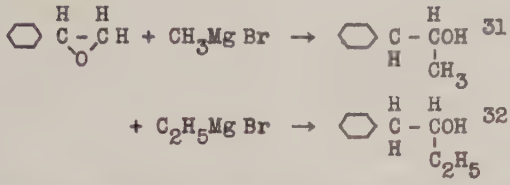
[27] Henry, Ber., 39, 3677 (1906).

[28] While this reaction is the reverse of which would have been predicted, if it is assumed that the product was properly identified, it is readily explainable on the basis of electromers, as in the previous reaction of propene oxide and HCl (loc. cit.).

[29] Tiffeneau and Fourneau, Compt. rend., 145, 437 (1907).

[30] Ibid., 146, 697 (1908).

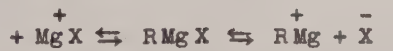
reactions, and that in certain cases the aryl group will cause a rearrangement to the aldehyde group before reaction, and in other cases it will react like the simple oxide. The alcohols which they obtained in these reactions follow:



Because it was felt that all the results given above were not in keeping with the theory of partial polarity which explains so well a number of other reactions, and since, too, the addition products of oxides were not proved beyond all doubt in a number of instances, it seemed well to investigate these reactions more critically, using the Grignard reagent as the basis of investigation. Furthermore, because of the definite electronegativity of the phenyl radical, it was decided to use not only styrene oxide but also phenyl magnesium bromide, and to determine if these reacted according to the theory which had been advanced by Tiffeneau.

REACTIONS OF STYRENE OXIDE WITH THE GRIGNARD REAGENT

It has already been pointed out that the Grignard reagent may dissociate in two ways:



If R is weakly electronegative, the dissociation goes to right, while if R is strongly electronegative, the dissociation goes to the left. In order to have the dissociation in this way only, the phenyl and anisyl radicals were employed.

In the case of styrene oxide, the presence of the strongly electronegative radical in the molecule will have a definite effect on the electrons of the oxygen-carbon bond. As has already been pointed out its effect is to push the electrons farther out towards

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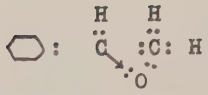
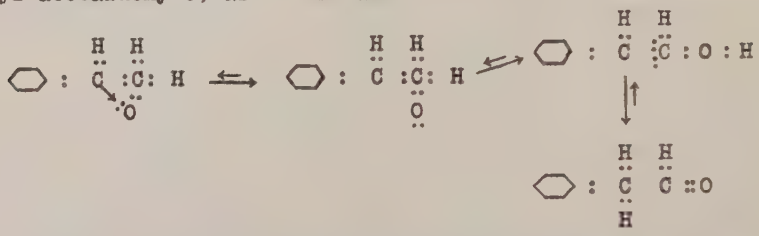
[31] This alcohol was identified by the preparation of the corresponding phenyl urethane derivative, which gave a M. P. 92°.

[32] This alcohol was identified by oxidation to the corresponding ketone, and the semicarbazone prepared, M. P. 153°.

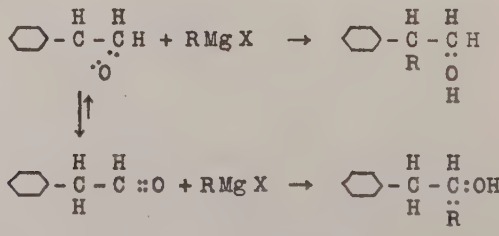
the oxygen thus:



This will produce a strain in this molecule, and the electrons may finally become so far removed from the carbon atom that the slightest application of energy will displace them completely toward the oxygen atom. If this occurs, a hydrogen will move off from the primary carbon to satisfy the oxygen, and phenyl vinyl alcohol will be formed. This latter compound is the tautomeric form of phenyl acetaldehyde, as illustrated:



In a solution containing all these forms the Grignard reagent will add with extreme rapidity to the aldehyde. If, then, the Grignard reagent be added slowly to a solution of the oxide of a structure which favors the aldehyde form, it will react instantly with the aldehyde thus destroying the oxide-aldehyde equilibrium. More aldehyde will then be formed which will, in turn, react with more of the Grignard reagent as it is added. If, on the other hand, the Grignard reagent is present in excess both the normal reaction and the reaction with the aldehyde will occur simultaneously. But, due to the relatively large proportion of the oxide present the normal reaction will exceed that of the aldehyde form.



PREPARATION OF 1,2-DIPHENYL ETHANOL

In order to test out the hypothesis advanced above, phenyl magnesium bromide was added slowly to a solution of the oxide in

ether. According to our hypothesis this should give the symmetrical diphenyl ethanol. Upon the isolation of the product of the reaction a yellow oil was obtained which was soluble in a number of organic solvents. Upon crystallization from dilute alcohol, a small portion of this oil yielded long, white, needle-like crystals, melting at 62°. This product was identified as the symmetrical diphenyl ethanol. Upon standing a short time the yellow oil described above became impregnated with a large quantity of crystals.

IDENTIFICATION OF THE 1,2-DIPHENYL ETHANOL

In Fig. 1 is given an outline of the procedure employed in the identification of this compound. An attempt to purify the oil by vacuum distillation resulted in the decomposition of the material with the loss of water, and the formation of a solid material which melted at 125° and proved to be stilbene. Furthermore, treatment with oxalic acid gave a large quantity of stilbene, and heating with phosphorus pentoxide yielded the same material. The reaction with oxalic acid and phosphorus pentoxide consisted merely of the loss of a molecule of water from the symmetrical diphenyl ethanol.

In order to prove definitely that the reaction which was postulated, namely the addition through the aldehyde form, actually occurred, and that it could not be reversed by the presence of an excess of Grignard reagent, the reaction was carried out in the proportions of two moles of Grignard to one of the oxide. Upon working up the oil as before (See Fig. 2.) identical results were obtained. In both cases the oil was oxidized to see if any benzophenone could be detected. However, although there was a little benzophenone formed in each case, the quantity of the unsymmetrical alcohol must have been very small. Moreover, the theory predicts that addition of the Grignard reagent would produce both products, although the quantities formed should vary with the mode of addition of the reagents.

PREPARATION OF 1,1-DIPHENYL ETHANOL-2

The findings described above corroborate, therefore, the hypothesis advanced. Further substantiation may be obtained by the addition of styrene oxide to the Grignard reagent. This should give us not the symmetrical alcohol but the unsymmetrical

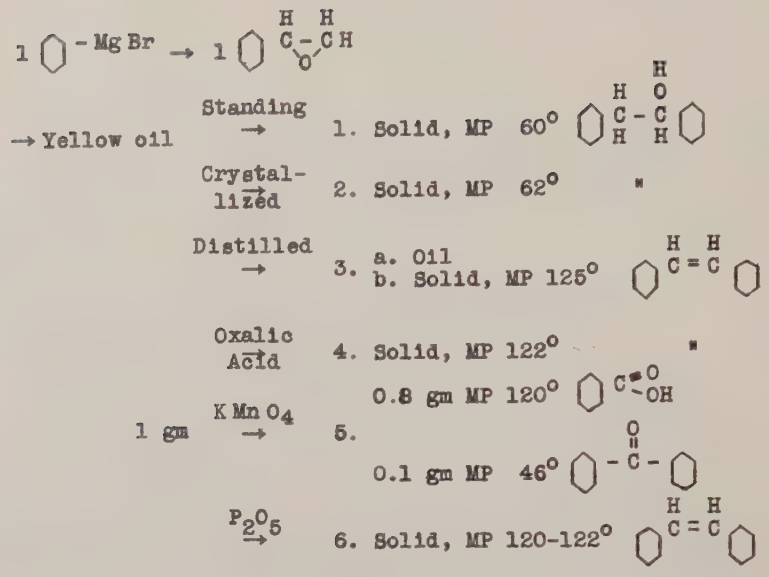

1 - Mg Br → 1
→ Yellow oil
Standing →
1. Solid, MP 60°
Crystal-lized →
2. Solid, MP 62°
Distilled →
3. a. Oil
b. Solid, MP 125°
Oxalic Acid →
4. Solid, MP 122°
1 gm
K Mn O4 →
5.
0.8 gm MP 120°
0.1 gm MP 46°
P2O5 →
6. Solid, MP 120-122°

Fig. 1

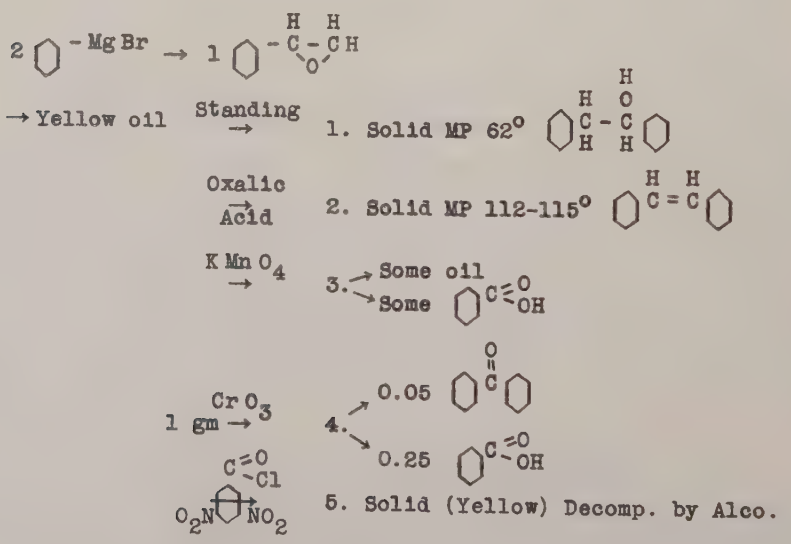

2 - Mg Br → 1
→ Yellow oil
Standing →
1. Solid MP 62°
Oxalic Acid →
2. Solid MP 112-115°
K Mn O4 →
3. Some oil
Some
1 gm
Cr O3 →
4.
0.05
0.25
5. Solid (Yellow) Decomp. by Alco.

Fig. 2

diphenyl ethyl alcohol according to the theory advanced on page 13. These conclusions were substantiated by the experiment described below.

Thus when one mole of styrene oxide was added to one mole of the Grignard reagent, and the product of the reaction isolated, a thick brown oil was obtained which was fairly soluble in organic solvents. This oil would not crystallize and appeared to be stable towards heat. The structure of the material was determined in the following manner. (See Fig. 3.)

The material was oxidized with strong alkaline permanganate solution, and the products of the oxidation isolated. It was found to yield mainly benzophenone; and some benzoic acid. The oil was heated with phosphorus pentoxide, and a large quantity of dark colored material was obtained, from which was isolated a very small amount of stilbene, which was identified by its melting point.[33] Some of the oil was heated with oxalic acid, and upon purification of the product from glacial acetic acid, beautiful white flaky crystals of M. P. 161° were obtained. These facts pointed to the conclusion that the material was the unsymmetrical diphenyl alcohol.

A second lot of the material was prepared, using in this case two moles of the Grignard for each mole of the oxide. This material was worked up as before and gave the same results (Fig. 4) as the material formed by 1:1 addition. Some of this material was treated with 3,5-dinitro benzoyl chloride in the hope of obtaining a solid derivative, and a white crystalline product was obtained M. P. 135°. It was concluded that the oil was the unsymmetrical diphenyl ethanol from a consideration of the following reactions. Benzophenone was the main product obtained upon oxidation. The oil yielded an oxalic acid ester instead of losing water when heated with oxalic acid. It was able to form a stable 3,5-dinitro benzoate whose melting point differed by 20 or more degrees from that of the unstable 3,5-dinitro benzoate of the symmetrical diphenyl ethanol.

PREPARATION OF 1,2-PHENYL P-ANISYL ETHYLENE

The p-anisyl compound was obtained by the addition of the

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[33] The fact that stilbene was isolated here merely proves the presence of a small quantity of the symmetrical diphenyl ethanol.

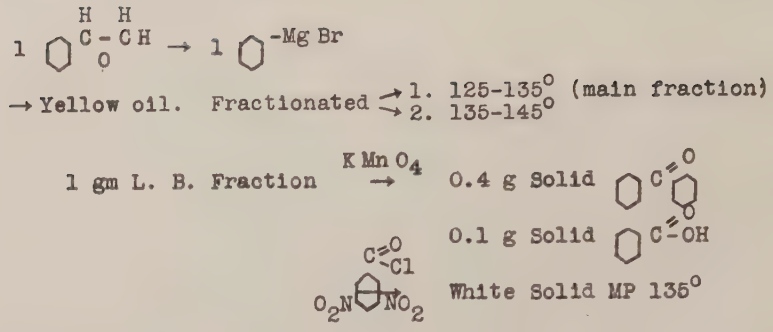
1
-Mg Br
→ Yellow oil. Fractionated → 1. 125-135° (main fraction)
→ 2. 135-145°
1 gm L. B. Fraction
K Mn O4
0.4 g Solid
0.1 g Solid
White Solid MP 135°

Fig. 3

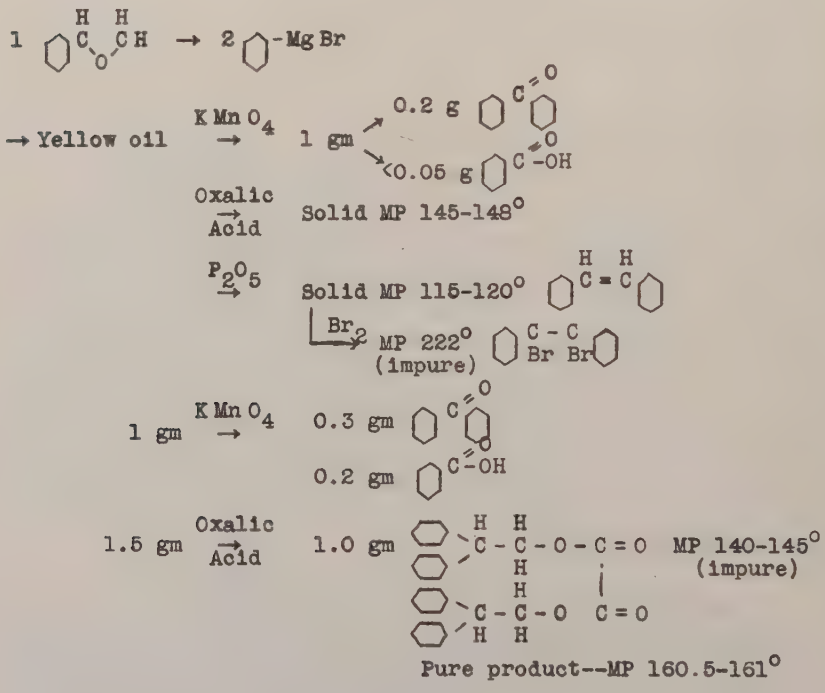
1
2
-Mg Br
→ Yellow oil
K Mn O4
1 gm
0.2 g
<0.05 g
Oxalic Acid
Solid MP 145-148°
P2O5
Solid MP 115-120°
Br2
MP 222° (impure)
1 gm
0.3 gm
0.2 gm
1.5 gm
1.0 gm
MP 140-145° (impure)
Pure product--MP 160.5-161°

Fig. 4

Grignard reagent to an equimolecular quantity of the oxide dissolved in ether. Upon isolation of the product a heavy viscous brown oil was obtained which was readily soluble in organic solvents, and would not crystallize. Upon standing, however, a crystalline material precipitated (See Fig. 5) which upon purification gave a melting point 127-130°. This material was identified as the phenyl p-anisyl ethylene. The oil which remained behind was oxidized in an attempt to isolate some of the phenyl anisyl ketone, but none was obtained. It should be noted here that the literature reports that the alcohol formed from benzyl magnesium chloride and benzaldehyde break down, and only the unsaturated derivative is obtained. These facts then substantiate those already obtained and support the theory advanced for the reactions of oxides.

PREPARATION OF 1,1-PHENYL, P-ANISYL ETHANOL-2

As a final test for the theory, the p-anisyl magnesium bromide was prepared, and styrene oxide was added to it in the ratio of one mole of oxide to two of the Grignard reagent. The product isolated was a thick brown oil, very similar in general appearance to that prepared before. But this material would not crystallize, and on standing for two weeks had not precipitated any appreciable quantity of material. (See Fig. 6.) Furthermore, treatment with phosphoric anhydride gave no crystalline material, and treatment with oxalic acid gave a small amount of impure material which melted at 55-60°. Upon oxidation the material yielded some phenyl anisyl ketone, and a small amount of mixed benzoic and anisic acids. From the formation of the ketone it was argued that the unsymmetrical molecule was present. This then indicates splitting by the Grignard reagent of the carbon oxygen bond in the manner anticipated by the theory.

IDENTIFICATION OF BIS-1,1-DIPHENYL ETHYL-2 OXALATE

The white crystalline material obtained from the reaction of the symmetrical diphenyl ethanol was identified as shown in Fig. 7. It was suspected that the material might be either an oxalate, a formate, or an isomeric form of stilbene. The material was, therefore, analyzed by the microcombustion method. From the results obtained, it was evident that the material was either the oxalate or the formate of diphenyl ethanol. To identify which

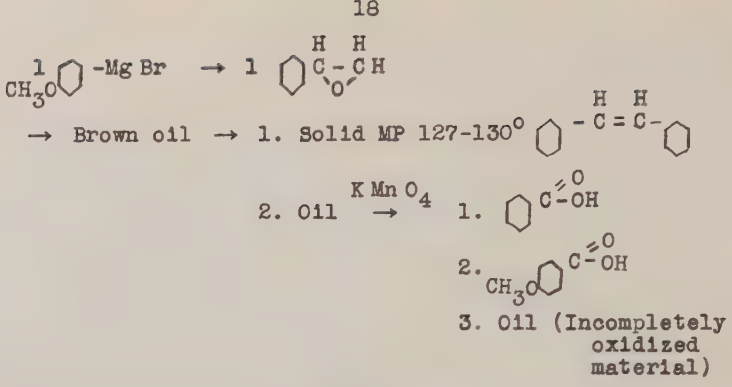

Fig. 5

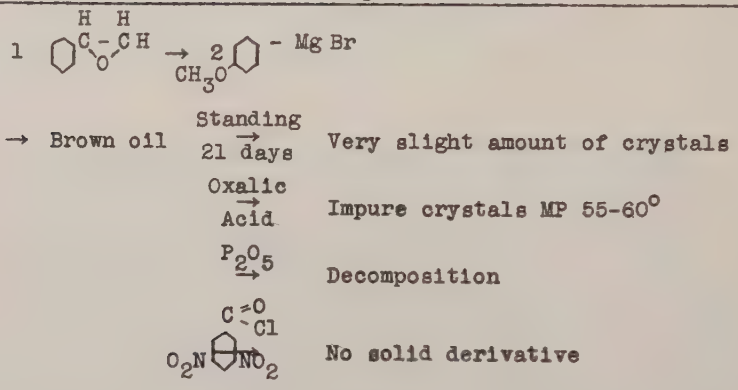

Fig. 6

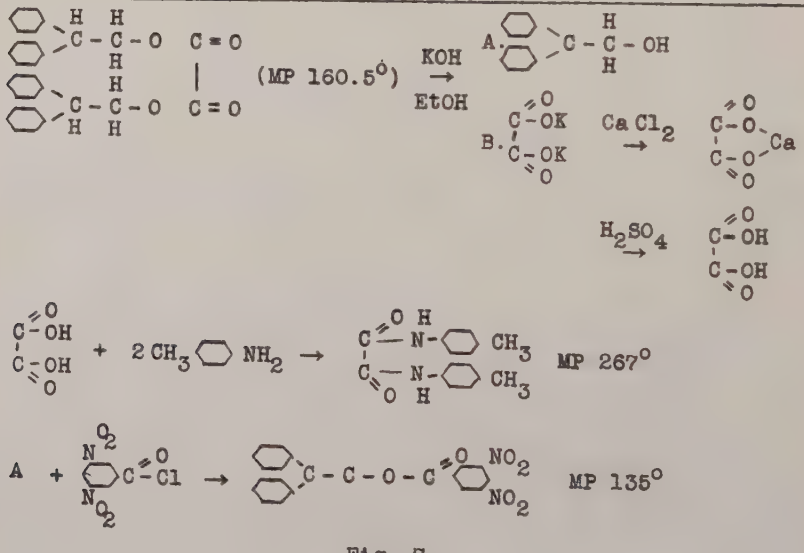

Fig. 7

ester was present in the molecule the material was saponified with alcoholic potassium hydroxide, and the liberated acid shown to be oxalic and identified by precipitation of the calcium salt, and formation of the toluide M. P. 267°. The alcohol residue was converted into the 3,5-dinitro-benzoate, and from its melting point (135°) it was shown that it had suffered no decomposition during the reaction with oxalic acid, since it agreed with the melting point of the material obtained from the treatment of the original oil with 3,5-dinitro benzoyl chloride.

These results, then, offer evidence for the correctness of the theory of the reaction of oxides. The reaction when a strongly electronegative group is present should at all times yield two products, and the amount of each product formed may be controlled by controlling the mode of addition of the reagent.

EXPERIMENTAL PART

PREPARATION OF OXIDES

In the preparation of the styrene oxide by the first method, a solution of HOBr was prepared by the reaction of mercuric oxide on a cold water solution of bromine. Freshly precipitated mercuric oxide and bromine were added in portions to a volume of cold water, while stirring vigorously with a mechanical stirrer. The solution of HOBr thus obtained was decanted from the solid material into a large separatory funnel. Freshly distilled styrene was added (25 grams), and the mixture shaken vigorously for several minutes. After a time an oil sank to the bottom, and the reaction was assumed to be complete. The material was now extracted with three portions of ether, washed rapidly with bicarbonate solution to remove any dissolved bromine, then washed with water and dried over sodium sulfate. The material was placed in a flask equipped with a stirrer and a reflux condenser, powdered potassium hydroxide added, and the material stirred vigorously overnight. The ether solution was then filtered, washed thoroughly with water, and dried over sodium sulfate. The ether was removed by the use of a column, and the oxide fractionated in vacuo at 10-15 mm., and the fraction retained which boiled between 80-90°. This material was found to weigh 20 grams.

Upon fractionation with a column at atmospheric pressure, that fraction was taken as pure which came over between 188-189°. This comprised 15 grams of material or a 52 per cent yield. When

tested for halogens, it gave a distinct Beilstein test. Its refractive index was taken with an Abbé refractometer, and was found to be N^{20}_{D} 1.5397 at 20°, while for water taken at the same time it was found to be N^{20}_{D} 1.3333.

The benzoyl hydroperoxide used in the second method[34] was prepared according to the directions given in "Organic Syntheses." One hundred twenty grams of benzoyl peroxide were dissolved in a liter and a half of dry toluene. The reaction was carried out in a large flask, equipped with a stirrer and a dropping funnel. The solution was cooled with an ice-salt mixture, and a cold solution of sodium ethylate was added. The material was then decomposed with two liters of ice water, the water layer separated and the ethyl benzoate completely extracted with cold ether. The water solution of the sodium benzoyl hydroperoxide was returned to the reaction flask, again cooled with an ice-salt bath, and then decomposed with 105 grams of ice-cold 50 per cent sulfuric acid. The water solution was extracted three times with cold chloroform, the chloroform solution dried over sodium sulfate and analyzed for total available oxygen. It was found that the best yields were obtained if the toluene was dried over sodium; and the chloroform used distilled and dried with anhydrous potassium carbonate, which would also remove any hydrochloric acid present.

The method pursued in utilizing this benzoyl hydroperoxide is also taken from "Organic Syntheses."[35] The yield from 120 grams of benzoyl peroxide was found to be 39 grams. Twenty-seven grams of styrene were added to the cold chloroform solution. The material was kept in an ice bath and vigorously agitated for the first hour. At the end of this time the material was placed in the ice chest for 24 hours. The solution was then washed first with an excess of cold dilute sodium hydroxide solution, and then several times with water, until free of alkali. The chloroform was then distilled off carefully and the oxide fractionated as in the above method, retaining the fraction boiling between 80-90° at 10-15 mms. This material amounted to 21 grams of the impure oxide. Upon fractionation at ordinary pressure, 12-15 grams of the pure oxide were obtained boiling between 188-189°. The refractive index was obtained with the Abbé refractometer and the reading was N^{20}_{D} 1.5357, and for water N^{20}_{D} 1.3333. Following the procedure

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[34] "Organic Syntheses," 8, 30 (1928).

[35] Ibid., 102 (1928).

outlined above it was possible to check the index of refraction of the oxide upon subsequent runs.

PREPARATION OF 1,2-DIPHENYL ETHANOL

In all the preparations given below involving the use of the Grignard reagent, the apparatus consisted of a small, three-necked flask, equipped with a condenser, a mercury sealed stirrer, and a dropping funnel. The condenser and dropping funnel were equipped with calcium chloride tubes and the apparatus was scrupulously clean and dry at all times. Absolute ether was used throughout.

The Grignard reagent was prepared from 7.2 grams of phenyl bromide and 1.1 grams of magnesium and added slowly, with vigorous stirring, to a solution of 5 grams of styrene oxide dissolved in ether and cooled with an ice bath. After all the material was added the reaction mixture was refluxed for one hour, again cooled with an ice bath and then decomposed, first with ice water, and then with a little dilute sulfuric acid. The ether solution was then separated, the water solution extracted twice more with ether, the extracts combined, washed, and the ether removed by evaporation in a vacuum desiccator.

REACTIONS OF 1,2-DIPHENYL ETHANOL-2

A yellow oil was obtained which upon crystallization from dilute alcohol yielded a product crystallizing in long, white needles, and giving a melting point of 60°. Moreover, upon standing, this crystalline material separated from the oil in large quantities. Upon treatment with oxalic acid and crystallization of the product from alcohol a white material was obtained, melting point 120°, which was found to be stilbene. Upon oxidation with alkaline permanganate solution there was obtained considerable benzoic acid and an oil, which was assumed to be unoxidized material. No benzophenone was obtained.

A second lot of this material was prepared, and it was attempted to purify the oil by fractional distillation. Although a very high vacuum was used, the oil decomposed considerably yielding a large quantity of stilbene, which, upon crystallization gave a melting point of 125°.

A third lot of this material was prepared in the same manner as before. Upon oxidation with alkaline potassium permanganate solution one gram of the oil yielded 0.8 of a gram of

benzoic acid and 0.1 of a gram of benzophenone. Some of the material, upon treatment with oxalic acid, working up and crystallizing from alcohol, yielded white crystals, melting point 120-122° which indicated that this material was stilbene.

PREPARATION OF 1,1-DIPHENYL ETHANOL-2

In the preparation of this material, the procedure was identical with the one described for the symmetrical diphenyl ethanol, except that in this case the oxide was added slowly to the solution containing the Grignard reagent. Upon removing the solvent, a product remained behind in the form of a yellow oil. The material was extremely soluble in ether, alcohol, acetone, benzene, petroleum ether, chloroform, and glacial acetic acid. It was impossible to crystallize the material from any of these solvents. The material was fractionated at 2 mms. pressure and collected in two fractions, boiling point 125-135° and 135-145°.

REACTIONS OF 1,1-DIPHENYL ETHANOL-2

Attempts to oxidize this material with chromic anhydride-glacial acetic acid mixture and with neutral potassium permanganate gave very poor results. For this reason the material was refluxed with an alkaline permanganate solution for three hours. The solution was then extracted with ether which, upon evaporation, yielded 0.4 grams of benzophenone, melting point 46°. The water solution, upon acidification, yielded 0.1 grams of benzoic acid. The benzoic acid was obtained by ether extraction and evaporating the ether in a vacuum desiccator.

A second lot of the same material was prepared in the manner outlined above, except that two moles of Grignard reagent were used for one mole of the oxide. The same thick yellow oil was obtained identical with that yielded by the reactions just described.

One gram of this material was oxidized by an alkaline permanganate solution yielding 0.2 of a gram of benzophenone, 0.05 of a gram of benzoic acid, and some oil, which indicated that the oxidation was not yet complete.

A small quantity of the oil was heated with anhydrous oxalic acid. The material turned dark brown and after washing out the excess of acid with water, was crystallized by the addition of alcohol, which dissolved a gummy material leaving a light yellow

crystalline product. This material melted at 145-148°, and upon crystallization from glacial acetic acid yielded a white, flaky crystalline product, melting point 160.5°.

Upon treatment of a small quantity of the original oil with phosphorus pentoxide a brown, tarry mass was produced which, upon washing with hot water and crystallization from alcohol yielded an extremely small quantity of impure stilbene, melting point 115-118°. Upon treatment of the stilbene with a chloroform solution of bromine a stilbene dibromide was obtained, which melted at 222°. This reaction, as well as the former indicates that the unsymmetrical diphenyl ethanol is contaminated with a small quantity of symmetrical diphenyl ethanol.

A third lot of the material was prepared in the manner last described. In this case 2.5 grams of the oxide yielded 3.7 grams of the oil. One and five-tenths grams of this oil was heated with one gram of anhydrous oxalic acid. At first a double layer formed which disappeared when heated for five minutes. The material was cooled, washed twice with water and once with alcohol, leaving a white crystalline product. This material was crystallized from glacial acetic acid and gave 1.0 of a gram of material, melting point 160.5°.

Two-tenths of a gram of the oil was treated with phosphorus pentoxide and left a black, tarry residue. This material was extracted with ether, evaporated and a crystalline residue obtained. This residue was crystallized from alcohol and about 0.05 grams of stilbene were thus obtained, of M. P. 118-120°.

One gram of the oil was refluxed for four hours with an excess of alkaline permanganate solution. Upon working up the material in the usual manner, there was obtained 0.3 grams of benzophenone, melting point 47°, and 0.2 grams of benzoic acid.

PREPARATION OF 1,2-PHENYL P-ANISYL ETHYLENE

This material was prepared by the general procedure outlined above. The Grignard from 8.6 grams of p-brom anisole was added to five grams of the oxide. The product was isolated as a viscous brown oil, which would not crystallize from alcohol or ether. When kept for a month, the material separated into a mass of pasty crystals. These were obtained by absorbing the oil on a porous plate. The material was crystallized from hot alcohol and melted at 130° which corresponds closely to that of the phenyl

anisyl ethylene (136°). Moreover, the alcohol which should be prepared from the use of the Grignard of benzyl chloride on anisaldehyde has never been isolated, since it goes over to the unsaturated compound. This evidence seems conclusive for the formation of this alcohol which then eliminates water to give the unsaturated derivative.

OXIDATION OF 1,2-PHENYL P-ANISYL ETHYLENE

Upon oxidation of the oily residue obtained by removal of the 1,2-phenyl p-anisyl ethylene, none of the corresponding ketone was obtained but merely a mixture of benzoic and anisic acids and a small quantity of unoxidized material. This seemed conclusive evidence for the formation in this case of the symmetrical product by means of the aldehyde type of reaction. These facts further substantiate the theory.

PREPARATION OF 1,1-PHENYL P-ANISYL ETHANOL-2

The Grignard reagent was prepared from 8.6 grams of the p-brom anisole and 1.1 grams of magnesium. The oxide was added slowly, and the procedure from then on was as usual. A thick brown oil was obtained, which was readily soluble in most organic solvents, and which would not crystallize from any solvents. The yield was 8 grams. Although this oil stood three weeks only a trace of crystalline material had separated.

REACTIONS OF 1,1-PHENYL P-ANISYL ETHANOL-2

When treated with phosphorus pentoxide, the material decomposed badly, and no crystalline material was isolated. Upon treatment with oxalic acid, the material which resulted was very gummy, and difficult to crystallize or purify. A small quantity of the material was obtained which gave a melting point of 55-60°, but was not sufficiently pure for analysis.

One gram of the oil was oxidized with alkaline permanganate solution, and when extracted with ether and evaporated, gave 0.4 grams of a light yellow oil which upon seeding with a little phenyl p-anisyl ketone, changed over to a white crystalline product, which gave a melting point 50-55°, and was shown by mixed melting point to be phenyl p-anisyl ketone. One gram of the materiel upon oxidation yielded 0.4 grams of the ketone, and 0.1 grams of mixed anisic and benzoic acids.

These facts showed that the material was the unsymmetrical phenyl p-anisyl ethanol which was predicted by the theory. The presence of a small quantity of 1,2-phenyl p-anisyl ethylene is indicated by the formation of the slight amount of crystalline material.

PROOF OF STRUCTURE OF PRODUCT OF CONDENSATION OF OXALIC ACID AND 1,1-DIPHENYL ETHANOL-2

This product was thought to be either the oxalate or the formate of 1,1-diphenyl ethanol-2 or else an isomeric form of stilbene.[36] This material was, therefore, analyzed by the micro-combustion method with the following results:[37]

Analyses. (Wts. given are in mgs.)

Subs., 4.104: CO_2, 11.98; H_2O, 2.26, Calc. for $C_{30}H_{26}O_4$: C, 80.00; H, 5.80. Found: C, 79.61; H, 6.16.

These results eliminated the polymeric stilbene, and it was now necessary to decide between the oxalate and the formate. Four-tenths grams of the material was refluxed for four hours with alcoholic potassium hydroxide. The alcohol was then evaporated, water added, and the material filtered to remove the oil. Calcium chloride solution was added to the filtrate and gave a white precipitate which remained in the presence of dilute acetic acid. This test was fairly good evidence for the presence of oxalate ion. The remainder of the solution was concentrated, acidified with dilute sulfuric acid and extracted four times with ether. Upon evaporation of the other a white crystalline material remained. This was heated with p-toluidine and crystallized from hot alcohol. The material melted at 266-267° while the same derivative prepared from pure oxalic acid in the same manner gave the same melting point and mixed melting point. The oil from this saponification was then warmed with 3,5-dinitro benzoyl chloride and the material crystallized from hot alcohol. Upon recrystallization the material melted at 135°. The original oil, when treated with 3,5-dinitro benzoyl chloride, also gave a product, M. P. 135°. This indicates that there has been no decomposition of the alcohol during the treatment with oxalic acid.

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[36] Such a polymer is reported in the literature (Ber., 42, 4871) M. P. 163°.

[37] This combustion was obtained through the courtesy of Dr. Wintersteiner. He states that at this time hydrogen was running approximately 0.3 per cent high.

SUMMARY

A theory has been advanced, based upon the work of Kharasch and Marker[38] which explains the reactions of oxides. This theory is applied to the reactions of oxides towards acids, salts, and the Grignard reagent. Discrepancies between the results obtained, and those which should be theoretically possible are pointed out.

The reactions of styrene oxide towards the Grignard reagent are investigated, using phenyl magnesium bromide and p-anisyl magnesium bromide. This work proves definitely that the mode of addition of the Grignard reagent determines whether the reaction will proceed in the normal manner as predicted by the theory of partial polarity, or whether the reaction will proceed through the removal of the isomeric aldehyde. If the oxide is present in excess the aldehyde reactions predominate. If the Grignard reagent is present in excess, the oxide reacts in the normal manner.

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[38] Loc. cit.

PART II

INTRODUCTION

This work was undertaken with the hope of preparing certain organic derivatives of lead which would be capable of giving water solutions, and at the same time would be of therapeutic value in the treatment of cancer. While colloidal lead preparations were being investigated quite extensively and with some success by Bell[1] in England, there were, however, several objections to the use of this material. Chief among these may be cited the following: toxicity, instability, lack of specificity and uniformity, and finally, difficulty of preparation. If, then, it were possible to prepare a series of water soluble organic lead derivatives, it seemed quite probable that they might retain their effectiveness for cancer control, and by varying the groups attached, render them more specific and less toxic than colloidal solutions of lead. It was hoped too, that if such derivatives might be prepared, that they would prove valuable as a therapeutic agent in other lines besides the control of cancer.

STABILITY OF ORGANO LEAD COMPOUNDS

With the general statement of the theory of partial polarity given in the first part of this paper as a foundation, it will be attempted to correlate the decomposition of the organo-lead derivatives with the relative electronegativity of the radicals attached. It has already been pointed out by Kharasch and others,[2] that the stability of symmetrical mercurials depends upon the relative electronegativity of the groups attached to the mercury. Thus if we have a mercurial of the type R Hg R, such as diphenyl, in which the groups are strongly electronegative, the resulting compound is stable towards heat. If, on the other hand, the radicals attached are weakly electronegative, as in the case

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[1] Bell, British Med. Jr., 1, 687-90 (1926). Lancet 1, 538-43 (1926).

[2] Kharasch and Stavely, J. Am. Chem. Soc., 45, 2961 (1923).

of the benzyl compound, the effect of heat is to displace the electrons toward the mercury with the result that dibenzyl and mercury are formed.

This theory fits in so well with the facts of the case when applied to mercurials, that it was deemed advisable to apply these concepts to lead derivatives as well. The lead derivatives are, however, somewhat more complex as they exhibit the valences of both two and four. The types to which this theory will be applied are accordingly,

Tetra-organo lead--PbR_4
Tri-organo salts--PbR_3X
Tri-organo lead--$R_3Pb:PbR_3$
Di-organo salts--PbR_2X_2
Di-organo lead--PbR_2

An inspection of the inorganic lead compounds leads to the conclusion that the stable form of lead is that in which it has the valence of two. This would mean that as two more groups, either of organic or inorganic nature are added to the lead, it is necessary for an extra pair of electrons to be pulled out from the lead. By application of the concept already stated in the case of mercury compounds, it is seen that this bond will be more stable if the radicals attached to the lead are strongly electronegative.

In the case of the tetra substituted inorganic salts such as lead tetrachloride, while the chlorine is highly electronegative the bond in this case is of the polar type, and the electrons are transferred completely to the chlorine, and not shared as in the case of the organic radicals. It is shown by Calingaert[3] that if tetra-ethyl lead is heated to 80° decomposition sets in, and that if heated to 135° the decomposition is explosive in nature. By comparing this with tetra-prenyl lead which is stable at its melting point 225°, it seems that the theory holds in general for the tetra organo derivatives. It may be pointed out too, that tetra-benzyl lead was not formed by the Grignard reaction even at low temperatures, but that dibenzyl was the product of the reaction.[4]

This theory finds even better support in the case of the tri-organo lead salts of the type PbR_3X. In this case a table

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[3]Calignaert, Chem. Revs. ,2, 54 (1925).

[4]This fact was ascertained by an attempt to prepare tetra benzyl lead.

taken from one by Caligaert[5] is given:

TABLE 1

FLUORIDES OF THE TYPE PbR_3F

Name of Salt	Temperature of Decomposition
Triphenyl lead fluoride	318°
Trimethyl lead fluoride	305
Tri p-tolyl lead fluoride	280
Tri-isoamyl lead fluoride	251
Triethyl lead fluoride	240
Tri n-propyl lead fluoride	235
Tri-isobutyl lead fluoride	230
Tricyclohexyl lead fluoride	198

It will be seen that all the radicals agree with the concept as stated for the stability of organo metallo derivatives. With a decrease in electronegativity[6] comes a decrease in stability within the molecule, with a correspondingly lower temperature of decomposition.[7] In the type of compounds, PbR_2X_2, the stability will depend both on R and X. But in this case the presence of the two non-polar bonds between lead and the inorganic radicals will be very similar to the condition existing in lead tetra chloride, and this class of compounds will be less stable than the tri-organo lead salts.

The tri-organo lead compounds of the type $R_3Pb:PbR_3$ are exceedingly interesting, resembling as they do the free radicals. When placed in the proper solvents they dissociate almost completely into two free radicals. As in the previous cases, it would be predicted on the basis of the theory of partial polarity, that the stability of these compounds would demand the presence of strongly electronegative groupings. This is particularly true for this class, in which the group as a whole must withstand the tendency to form tetra-substituted products, with the liberation of free

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[5] Calingaert, Chem. Revs., 2, 74 (1925).

[6] For a table of electronegativity of organic radicals, consult Kharasch and Reinmuth, Jr. Chem. Ed., 5, 407 (1918).

[7] The only radical which does not fall into its proper order is the p-tolyl. The electronegativity of this group would presuppose that this compound be more stable than the phenyl homologua. A cursory inspection of the preparation by Krause and Pohland seems to show that their compound was tri p-tolyl lead fluoride as claimed.

lead. The following table illustrates this:

TABLE 2[8]

DERIVATIVES OF THE TYPE $R_3Pb:PbR_3$

Name of Compound	Temperature of Decomposition
Tri o-tolyl lead	240°
Tri p-xylyl lead	220
Tri p-tolyl lead	193
Triphenyl lead	155
Triethyl lead	Room temp.

As was predicted, the more electronegative radicals only, namely those above phenyl were able to form this type of lead compound. In the case of ethyl, the material was never isolated, as it decomposed below room temperature.

What has been said for the tri-valent lead derivatives applies even more to the di-valent lead derivatives. For this type of compound to be stable, the electrons must be sufficiently displaced from the lead to withstand the tendency for two molecules to react, splitting out lead and yielding the tetra valent derivative. From the standpoint of the theory just advanced, the only bond which would be stable under these conditions would be one in which the electrons were held very firmly by the group attached. For this type of compound stability demands the presence of strongly electronegative groups. In coincidence with this theory it may be pointed out that Krause and Schmitz[9] have prepared diphenyl and di p-tolyl lead, and although attempts have been made to prepare diethyl and dibutyl lead,[10] they have met with no success.

QUATERNARY LEAD-SULFUR DERIVATIVES

In the case of the tri-organo lead salts, it has been shown that the stability of the compound varies with the anion present, provided the organo group attached is kept constant. Thus in the case of R_3PbX, the stability decreases with the substitution of decreasingly electronegative anions plus

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[8]Krause, Ber.,52, 2150 (1919); 55, 888 (1922).
[9]Krause and Schmitz, Ber., 52, 2150, 2165 (1919).
[10]Calingaert, Chem. Revs., 2, 70 (1925).

OH-F-Cl-Br-I.[11] It was decided, therefore, to examine derivatives of the type R Pb-S-R', to see whether the stability of the lead sulfur linkage would be sufficient to allow the isolation of this series of compounds. It was hoped by this method to prepare a series of water soluble derivatives since using the proper group R' would bring the whole molecule into solution.

When this investigation was undertaken compounds of the type R_3Pb-S-R were unknown. It was hoped that in the proper solvents thiosalicylic acid and thiosulfonic acid would combine with tri-organo lead chlorides, to give a lead sulfur linkage.

PREPARATION OF TRIETHYL LEAD THIOSALICYLIC ACID

Accordingly, triethyl lead chloride was dissolved in ethyl alcohol, and added to an equimolecular quantity of the thiosalicylic acid. Upon the addition of water, a white compound separated. This material was purified and analyzed for lead. But while the pure product should contain 46 per cent lead, analyses ran very much under this figure. Moreover, triethyl lead chloride was found to split off readily upon the addition of sodium chloride to the sodium carbonate solution.

A second attempt was made to prepare this type of compound using thiosulfonic acid in the place of thiosalicylic acid. In this case the triethyl lead chloride was dissolved in aqueous acetone solution, and added to the water solution of the thiosulfonic acid. The whole solution was then evaporated to dryness. The residue was tested for solubility in water and sodium carbonate solution.

A second attempt was made to prepare this type of compound using thiosulfonic acid in the place of thiosalicylic acid. In this case the triethyl lead chloride was dissolved in aqueous acetone solution, and added to the water solution of the thiosulfonic acid. The whole solution was then evaporated to dryness. The residue was tested for solubility in water and sodium carbonate solution, and stability in the presence of sodium chloride. As in the previous case, triethyl lead chloride was precipitated from alkaline solution, and the material was not completely soluble in the water solution, indicating instability of the lead-sulfur bond.

From these facts, it was concluded that, although the bivalent lead-sulfur bond is of sufficient strength to withstand

[11] Ibid., 2, 73 (1925).

acids and alkalies, the nature of the quaternary valence of lead is entirely different, and a weaker bond exists in this case.

EXPERIMENTAL PART

PREPARATION OF THIOSALICYLIC ACID[12]

The thiosalicylic acid was obtained by dizaotization of 130 grams of anthranilic acid with 69 grams of sodium nitrite. This solution was then added to a cold solution of sodium polysulfide in alkali. The temperature was allowed to rise and the mixture acidified. The disulfide was filtered, washed, and dissolved in sodium carbonate solution. The sulfur was then removed by filtration, and the disulfide reduced by boiling with a sufficient quantity of zinc dust. The reduction was complete when acidification yielded an alcohol soluble product, and no odor of hydrogen sulfide. The material was then treated with the proper amount of sodium hydroxide, boiled and filtered. Upon acidification a white crystalline product was obtained of melting point 146°. The yield was good, and the product analyzed 95 per cent pure.

PREPARATION OF THIOSULFONIC ACID

This preparation was more difficult than the previous one, due to the ease with which the material is oxidized in the presence of air. After the reduction the material was protected from the air by keeping it under carbon dioxide. This was particularly true during filtration. The quantities used in the preparation are as follows:

209 grams sulfanilic acid
500 cc. 2N NaOH
100 grams sodium nitrite
300 cc. conc. HCl
200 grams potassium xanthate
2 grams copper bronze powder
40 grams zinc dust
40 grams sodium carbonate
20 grams sodium hydroxide
300 grams lead acetate

The sulfanilic acid was dissolved in the sodium hydroxide solution, the nitrite added, and diazotization effected by slow addition of the hydrochloric acid. The solution was neutralized with sodium bicarbonate, and the potassium xanthate added slowly.

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[12] Cain, Manufacture of Intermediate Products for Dyes, p. 149.

Copper dust was then added, and the solution allowed to rise to room temperature, boiled for half an hour, and filtered hot. The zinc dust and sodium carbonate were then added, and the material refluxed for three hours, while hydrogen was bubbled through the solution. The material was again filtered, fresh zinc dust and sodium hydroxide added, and the material refluxed for another hour. The solution was decanted, acidified with HCl, and the acid precipitated as the lead salt. The mixture was cooled slowly with occasional agitation, and then filtered. The precipitate was washed, suspended in water, and the lead precipitated as the sulfide. The material was filtered and the filtrate evaporated in vacuo, at low temperature. The free acid remained behind as a light yellow powder. Yield--moderate, 87 per cent pure by analysis.

PREPARATION OF TRIETHYL LEAD CHLORIDE

One-tenth mole of lead tetraethyl (32 grams) was placed in a flask containing 0.1 mole of hydrogen chloride in ethyl alcohol. The reaction started upon warming, and once started, proceeded vigorously in the cold. The triethyl lead chloride formed went into solution in the ethyl alcohol, and was obtained by precipitation with water. The material was washed and dried and crystallized from dilute alcohol.

ANALYSIS OF TRIETHYL LEAD CHLORIDE

The material was decomposed by concentrated sulfuric acid with the addition of some concentrated nitric acid. The material was heated until the reaction was complete. The sulfuric acid was then diluted, and the lead sulfate filtered through a prepared gooch crucible ignited and weighed as lead sulfate.

Analyses. Subs., 0.6285, 0.9629: $PbSO_4$, 0.5737, 0.8759. Calc. for $C_6H_{15}PbCl$: Pb,62.7. Found: 62.21, 62.13.

PREPARATION OF TRIETHYL LEAD THIOSALICYLIC ACID

Five grams of the triethyl lead chloride were dissolved in alcohol, and added to a solution of 2.6 grams of thiosalicylic acid in alcohol. The material was allowed to stand for a short time, and then precipitated by the addition of water. The material was dissolved in sodium carbonate solution and tested with sodium chloride to determine whether any free triethyl lead

chloride was present. Upon addition of an excess of sodium chloride a slow precipitation of triethyl lead chloride was observed. This was an indication that slow hydrolysis was taking place.

ANALYSIS OF THE TRIETHYL LEAD THIOSALICYLIC ACID

The white material was analyzed to determine whether it was the pure mercaptan or not. The analysis gave the following results, indicating that it was impure:

Analyses. Subs., 0.4002, 0.4032, 0.2687: $PbSO_4$, 0.2168, 0.2425, 0.1666. Calc. for $C_{13}H_{20}O_2SPb$: Pb, 46.4. Found: 38.7, 41.1, 42.3.

PREPARATION OF TRIETHYL LEAD THIOSULFONIC ACID

An acetone solution of 5 grams of triethyl lead chloride was prepared and water was added until the material just commenced to precipitate. Two and nine-tenths grams of the thiosulfonic acid were dissolved in a little water and added to the triethyl lead chloride solution. The new solution was evaporated, and the residue dissolved in water. A slow precipitation of triethyl lead hydroxide occurred, while upon addition of sodium chloride solution the precipitation was more rapid.

SUMMARY

A theory has been advanced which correlated the thermal stability of organo lead derivatives with the type of radicals attached. This theory is applied successfully to all the types of organo lead derivatives.

Some derivatives of the type $R_3Pb\text{-}S\text{-}R'$ are prepared, and the stability of this type of lead sulfur linkage is studied. It is shown that this bond is not comparable in stability with the lead sulfur linkage in lead sulfide, but undergoes hydrolysis very readily.